REMARKS

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks. The foregoing amendments are fully supported by the specification, at least, at page 2, lines 22-25, page 3, lines 3-7, page 7, lines 8-12, and throughout the examples. Although the exact words of the amendment do not necessarily appear in the specification, it is clear that the intent is to purify the L-amino acid away from the medium in the passages cited above. In addition, it is clear that the amount of L-amino acid produced is measured by comparing the production in a bacterium which does not contain the inventive DNA. Entry is respectfully requested as no new matter is added.

Request for Interview

Applicants respectfully request that if this submission does not place the application in condition for allowance, the undersigned be called and an interview is requested prior to the issuance of a final Office Action. The prosecution history in the application has been rather convoluted, particularly in light of the recent withdrawal of the appeal following the submission of Applicant's Appeal Brief. Such actions greatly increase the expense for Applieants, and therefore, an interview is respectfully requested prior to the issuance of a Final Rejection.

Amendments

Claims 1-76 have been cancelled. Claim 77 is amended. Claims 77-84 are pending and under examination.

Rejection under 35 U.S.C. § 103(a)

In the Office Action, beginning at page 3, Claims 77-84 were rejected under 35 U.S.C. § 103(a), as reciting subject matters that allegedly are obvious, and therefore allegedly unpatentable, over the disclosure of Kobayashi in view of Williams et al. and as evidenced by Zakataeva and Hanko et al. Applicant respectfully requests reconsideration of this rejection.

The claims are drawn to a method of producing an L-amino acid by 3 distinct,

manipulative steps. That is, step 1 is cultivating the bacterium, step 2 is removing solids including cells from the medium, and step 3 is purifying the L-amino acid from the medium obtained in step 2. These are distinct steps as indicated in the claim, for example, that the L-amino acid is purified from the medium obtained in the second step. Clearly, one cannot purify the L-amino acid recited in step 3 without first obtaining the medium in step 2, that is, a medium having the solids, including cells, removed. Contrary to the teachings of any of the cited references, the desired product, the L-amino acid, is purified from the supernatent, that is the medium, after removing solids, including cells, from the medium. This is explicitly stated in the claims, in that step B states that the solids, such as the cells and cellular debris, are removed from the culture medium, and step C states that the L-amino acid is purified from the medium obtained in step B). It is undisputed that this medium is the supernatent obtained after removing the cells and cellular debris.

It is asserted that the Examiner has made an error in interpreting the claims, and as a result, has mis-applied the prior art. Specifically, Kobayashi is cited for teaching an *E. coli* host cell transformed with vector pAB104, which comprises a DNA segment which includes the region between and including genes pldA and pldB (see p. 1012, figure 4 and p. 1014, figure 6). This region includes the DNA of SEQ ID NO: 3, which encodes the amino acid sequence of SEQ ID NO: 4, as demonstrated by Zakataeva. Appellants have agreed with this interpretation of these references.

The newly cited Williams et al. is cited as the secondary reference to Kobayashi, in that it is to make up for the acknowledged deficiency of Kobayashi of NOT teaching steps B) and C) of claim 74, for example, purification of an L-amino acid including L-threonine. Williams et al. is cited for teaching the centrifugation of an *E. coli* culture for 10 minutes, and that one of ordinary skill in the art would recognize that during centrifugation, the cells become forced to the bottom of the tube and become the cell pellet, while the liquid portion of the culture medium remains above the pellet. The evidentiary reference of Hanko et al. is cited to show that LB medium contains L-amino acids, as was commonly known in the art.

Despite the newly cited secondary and evidentiary references, it remains the Applicants position that Kobayashi fails to teach the recovery or purification of an L-

amino acid, nor even any indication that an L-amino acid might be present in the medium following the cultivation and centrifugation of the cultivated cells, and the evidentiary references fail to make up for this deficiency. It is for these and the following reasons that the Examiner's interpretation of the claims is in error.

Specifically, the Examiner has cited to the teaching in Kobayashi, on page 1009 in the section entitled "Enzyme Assay" at the bottom of column 1, that the strain harboring the desired vector is cultured, and then the cells are 'spun down' and washed. The pellet, which contains the solids such as the cells and cellular debris, was further processed and the objective enzymes were further purified from the processed pellet. The medium is not used for any purpose and is likely discarded, as it is NOT further processed. There is no disclosure of recovering any substance from the medium or supernatent that remains after the 'spinning'. There is no disclosure that any substance ***could be*** isolated from the medium or supernatent. More importantly, the reference of Kobayashi fails to teach, either explicitly or implicitly, step C of claim 1, that is, the purification of the L-amino acid from the medium obtained in step B.

The Examiner has stated that "by practicing the method of Kobayashi, one of ordinary skill in the art would be "removing solids" in accordance with step B and purifying said L-amino acid" in accordance with step C simultaneously." (see page 3 of the Office Action mailed April 16, 2007). The Examiner explains that the step of centrifuging the cells would simultaneously remove solids from the medium and purify the L-amino acid, which is in the cells, from the medium. This interpretation of the prior art and application to the claims is a clear error.

This is because the claims distinctly recite 3 manipulative steps, that is, cultivating the bacterium, removing solids including cells from the medium, and purifying the L-amino acid ***from the medium*** obtained in the second step. These are distinct steps as indicated in the claim, for example, that the L-amino acid is purified from the medium obtained in the second step. Clearly, one cannot purify the L-amino acid without first obtaining the medium in the second step, that is, a medium having the solids, including cells, removed. The Examiner has erred in interpreting steps B and C to be combined into one. It is clear that step C cannot be conducted without first obtaining the medium from step B. It is impossible to combine them for this reason. Merely

separating the pellet with the cellular debris from the medium cannot be interpreted as "purifying the L-amino acid ***from the medium"***, as the medium is only obtained as a result of this separation.

In the latest Office Action, the Examiner argues that the claim does not specify that ***all*** the cells would be removed from the medium, some may remain from which the L-amino acid would be purified, and that also, there are L-amino acids present in the LB medium as components of the medium which would likely be purified, thus satisfying the last two steps of the claimed method. However, the claims have been amended to recite that the L-amino acid to be purified is present in the remaining medium (after purification by centrifugation) is present in an amount larger than if the cells were cultured and not transformed. This is the crux of the invention not recognized by any of the cited prior art. Clearly, the references do not teach such an increase in amino acid production, nor would one of ordinary skill in the art expect such an increase based on the teachings of the references, either singly or combined.

Furthermore, Kobayashi teaches away from purifying L-amino acids from any cell culture since the only description of a culture method describes manipulation of the post-centrifugation pellet, which does not contain the objective L-amino acids. The term "purifying" as defined in the specification on page 23, lines 2-7 clearly indicates a manipulative step such as "ion exchange, concentration and crystalline fraction methods..." is performed, which is not described or suggested by the Enzyme Assay of Kobayashi. This represents a further clear error in the interpretation of the claim, as the Examiner has refused to read the claims' terms in light of the specification. Although it is acknowledged that the purification methods decribed in the specification at page 23 cannot be imported into the claim, Appellant's definition cannot be completely ignored. The Examiner is completely ignoring this definition in the specification, as it clearly indicates that the claim must be interpreted to actually indicate a purification of the amino acid from the medium, not merely separating a medium from a pellet, as is taught by Kobayashi.

The application of Williams et al. to the claims does not overcome the shortcomings of Kobayashi, in that there is still no teaching of purifying an amino acid from the aliquot or the medium after removing the solids from the medium. Furthermore,

one of ordinary skill must have a reason or motivation to combine the references (*KSR International Co. v. Teleflex Inc. et al.,* No. 04-1350, slip op. at 16 (S.Ct., April 30, 2007)), and there is no commonality in the teachings of these references that would provide a reason for the person of ordinary skill in the art to combine these teachings. Neither reference has the goal of producing an L-amino acid, nor discuss such production in reference to the methods taught. As neither reference teaches or suggests such a method or even the desire to obtain an L-amino acid, the methods taught by these references fail to render obvious the claimed method. There is no teaching in any of the 4 cited references of step C in the claimed method, nor any suggestion from the various teachings of centrifugation of the various cultures for the purpose of producing large amounts of a desired amino acid. Therefore, this reference adds nothing to the rejection and fails to render obvious the claimed invention.

For at least the foregoing reasons, Applicant respectfully submits that the subject matters of Claims 77-84, each taken as a whole, would not have been obvious to one of ordinary skill in the art at the time of Applicant's invention, are therefore not unpatentable under 35 U.S.C. § 103(a), and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 103(a).

In the Office Action, beginning at page 8, Claims 77-84 were rejected under 35 U.S.C. § 103(a), as reciting subject matters that allegedly are obvious, and therefore allegedly unpatentable, over the disclosure of Kobayashi in view of Williams and Kaplan et al. and as evidenced by Zakataeva and Kruse. Applicant respectfully requests reconsideration of this rejection.

The teachings and lack thereof relative to the present invention of Kobayashi, Williams, Zakataeva are presented above. The reference of Kruse has been discussed in previous responses and in the Appeal Brief. The citation of Kaplan is new, and is discussed *infra.* Kaplan is cited for showing that *E.coli* is a well-known L-threonine producer. This fact is not disputed and is well-known in the art. Therefore, this reference adds no further weight to the rejection and the arguments presented above continue to apply. Specifically, there would be no motivation or reason to isolate a markedly increased amount of L-threonine from the medium after purifying the cells after

centrifugation. In fact, as shown above, one of ordinary skill in the art would have assumed that the cells and all cellular products would be present in the pellet. Therefore, one of ordinary skill in the art would not have expected a large of amount of L-threonine in the medium at this point in the process of the claimed invention, and hence the invention is non-obvious over the cited prior art.

None of the references has the goal of producing an L-amino acid, nor discuss such production in reference to the methods taught. As none of the cited reference teaches or suggests such a method or even the desire to obtain an L-amino acid, the methods taught by these references fail to render obvious the claimed method. There is no teaching in any of the cited references of step C in the claimed method, nor any suggestion from the various teachings of centrifugation of the various cultures for the purpose of producing large amounts of a desired amino acid. Therefore, the Kaplan reference adds nothing to the rejection and fails to render obvious the claimed invention in combination with the other cited references.

For at least the foregoing reasons, Applicant respectfully submits that the subject matters of Claims 77-84, each taken as a whole, would not have been obvious to one of ordinary skill in the art at the time of Applicant's invention, are therefore not unpatentable under 35 U.S.C. § 103(a), and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 103(a).

In the Office Action, beginning at page 10, Claims 77-84 were rejected under 35 U.S.C. § 103(a), as reciting subject matters that allegedly are obvious, and therefore allegedly unpatentable, over the disclosure of Kobayashi in view of Kaplan, Georgiou et al., and Begot et al., as evidenced by Zakataeva and Kruse. Applicant respectfully requests reconsideration of this rejection.

The teachings and lack thereof relative to the present invention of Kobayashi, Williams, Kaplan, and Zakataeva are presented above. The references of Kruse and Georgiou have also been discussed in previous responses and in the Appeal Brief. The citation of Begot is new, and is discussed *infra*. Begot, similar to Georgiou, is cited for showing that it was well-known to determine the growth phase of a bacterial culture medium by monitoring the optical density of the medium. This fact is not disputed, but

fails to make up for the deficiencies of Kobayashi. Therefore, this reference adds no further weight to the rejection and the arguments presented above continue to apply. Specifically, there would be no motivation or reason to expect a markedly increased amount of L-threonine from the medium after purifying the cells after centrifugation. In fact, as shown above, one of ordinary skill in the art would have assumed that the cells and all cellular products would be present in the pellet. Of course, one might expect a very small amount of L-amino acid to be present in the medium, as it is known that LB medium contains amino acids. However, one of ordinary skill in the art would not have expected a large of amount of L-threonine in the medium at this point in the process of the claimed invention, and hence the invention is non-obvious over the cited prior art.

None of the references has the goal of producing an L-amino acid, nor discuss such production in reference to the methods taught. As none of the cited reference teaches or suggests such a method or even the desire to obtain an L-amino acid, the methods taught by these references fail to render obvious the claimed method. There is no teaching in any of the cited references of step C in the claimed method, nor any suggestion from the various teachings of centrifugation of the various cultures for the purpose of producing large amounts of a desired amino acid. Therefore, the Begot reference adds nothing to the rejection and fails to render obvious the claimed invention in combination with the other cited references.

For at least the foregoing reasons, Applicant respectfully submits that the subject matters of Claims 77-84, each taken as a whole, would not have been obvious to one of ordinary skill in the art at the time of Applicant's invention, are therefore not unpatentable under 35 U.S.C. § 103(a), and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 103(a).

Obviousness-type Double Patenting Rejection

In the Office Action, beginning at page 13, Claims 77-84 were rejected under the judicially-created doctrine of obviousness-type double patenting as reciting subject matters that are allegedly not separately patentable over the subject matters recited in Claims 4 and 6-7 of co-pending U.S. Patent Application No. 11/106,455. Applicant respectfully requests reconsideration of this rejection.

Although Applicants do not necessarily agree with the basis for the rejection, a Terminal Disclaimer is filed herewith to advance prosecution.

For at least the foregoing reasons, Applicant respectfully submits that the subject matters of Claims 77-84 are separately patentable over the subject matters of Claims 4 and 6-7 in the '455 patent application, and therefore respectfully requests withdrawal of the rejection thereof.

Conclusion

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Steadman believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, he is invited to call on the number below.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is hereby authorized to charge fees necessitated by this paper, and to credit all refunds and overpayments, to our Deposit Account 50-2821.

Respectfully submitted,

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